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Claims

1. Use of a peptide containing an essential ventricular myosin light chain type 1 (vMLC1) amino acid sequence, which is functional as cleavage site for caspase-3, in the screening for a compound for the treatment of chronic or acute cardiovascular disease.

2. Use according to claim 1, wherein the amino acid sequence is DFVE.

3. Use according to claim 1 or 2, wherein the peptide is vMLC1.

4. Use according to any one of the preceding claims wherein the screening is directed to a compound which selectively inhibits the caspase-3-mediated cleavage of vMLC1 under predetermined conditions while essentially not inhibiting the caspase-3-mediated cleavage of a protein containing a functional caspase-3 DEVD cleavage site under the same conditions.

5. Use according to claim 4, wherein the selectivity is based on the structure of the compound.

6. Use according to claim 4, wherein the selectivity of the compound is based on the concentration of the compound.

7. A screening method for inhibitors of the caspase-3-mediated cleavage of vMLC1, which comprises:
   (a) contacting a test compound and a sample containing
      (i) a peptide containing a vMLC1 amino acid sequence which is functional as cleavage site for caspase-3, and
      (ii) caspase-3,
      under predetermined conditions allowing cleavage of the peptide at the cleavage site in the absence of the test compound, followed by
   (b) determining the presence or absence of an inhibition of the protein cleavage activity at the cleavage site as compared to the absence of the test compound, and
   (c) identifying a compound as an inhibitor which provides for the presence of inhibition of the caspase-3-mediated cleavage of the protein in step (b).

8. A screening method for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site, which comprises:

(a) contacting a predetermined amount of an inhibitor identified or identifiable by the screening method of claim 7 and a sample containing

(i) a peptide containing a functional caspase-3 DEVD cleavage site,

(ii) caspase-3, and optionally

(iii) a peptide containing a functional caspase-3 vMLC1 cleavage site,

under predetermined conditions allowing cleavage of a peptide containing a functional caspase-3 vMLC1 cleavage site in the absence of the test compound, followed by

(b) determining the presence or absence of a change of the protein cleavage activity at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site as compared to the absence of the test compound, and

(c) identifying a compound as a selective inhibitor which provides at the predetermined concentration for an essential absence of a change of the protein cleavage activity at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site.

9. The method of claim 7, wherein the screening method for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site of claim 8 is simultaneously carried out.

10. The method of any one of claims 7 to 9, wherein the peptide containing a vMLC1 amino acid sequence which is functional as cleavage site for caspase-3 is vMLC1.

11. The method of any one of claims 7 to 10, wherein the peptide contains the sequence DFVE as amino acid sequence of essential ventricular myosin light chain which is functional as cleavage site for caspase-3.

12. A cell assay for screening for inhibitors of the caspase-3-mediated cleavage of vMLC1, which comprises

(a) providing a culture of isolated cardiomyocytes,

(b) introducing activated caspase-3 into cardiomyocytes of step (a),

(c) determining the presence or absence of a reduction of the extent of caspase-3-mediated cleavage of vMLC1 and/or an improvement of cell contractility under predetermined conditions in the presence of a test compound as compared to the absence of the test compound,

(d) identifying a compound as an inhibitor which provides for the presence of inhibition of the caspase-3-mediated cleavage of vMLC1 and/or for an improved cell contractility in step (c).

13. A cell assay for screening for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site, which comprises

(a) providing a culture of isolated cardiomyocytes,

(b) introducing activated caspase-3 into cardiomyocytes of step (a),

(c) determining the presence or absence of a change of the extent of protein cleavage at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site in the presence of a predetermined amount of an inhibitor identified or identifiable by the assay of claim 12 as compared to the absence of the inhibitor, and

(c) identifying a compound as a selective inhibitor which provides in the predetermined amount for an essential absence of a change of the protein cleavage at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site.

14. The assay of claims 12, wherein the assay for screening for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site of claim 13 is simultaneously carried out.

15. An *in vivo* assay for screening for inhibitors of the caspase-3-mediated cleavage of vMLC1, which comprises

(a) providing an animal model, preferably for heart failure,

(b) administering a test compound to the animal model of step (a),

(c) determining the presence or absence of a reduction of the extent of caspase-3-mediated cleavage of vMLC1 and/or an improvement of heart failure under predetermined conditions in the presence of the test compound as compared to the absence of the test compound,

(d) identifying a compound as an inhibitor which provides for the presence of inhibition of the caspase-3-mediated cleavage of vMLC1 and/or for an improvement of heart failure in step (c).

16. An *in vivo* assay for screening for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site, which comprises

(a) providing an animal model, preferably for heart failure,

(b) administering a test compound to the animal model of step (a),

(c) determining the presence or absence of a change of the extent of protein cleavage at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site in the presence of a predetermined amount of an inhibitor identified or identifiable by the assay of one of claims 7 to 15 as compared to the absence of the inhibitor, and

(d) identifying a compound as a selective inhibitor which provides in the predetermined amount for an essential absence of a change of the protein cleavage activity at the cleavage site of the peptide containing a functional caspase-3 DEVD cleavage site.

17. The assay of claims 15, wherein the assay for screening for selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site of claim 16 is simultaneously carried out.

18. The assay of any one of claims 15 to 17, wherein the determination in step (c) is performed based on a measurement of contractility of cardiomyocytes and/or Western blotting.

19. The assay of claim 12 or 15, wherein the reduction in the extent of caspase-3-mediated cleavage of vMLC1 is determined by detection of a specific cleavage product of caspase-3-mediated cleavage of vMLC1, notably by Western blotting.

20. Kit-of-parts for identifying inhibitors of the caspase-3-mediated cleavage of vMLC1 according to claim 7, comprising the following components:

(i) a first component comprising a peptide containing an essential ventricular myosin light chain amino acid sequence, which is functional as cleavage site for caspase-3, and

(ii) a second component comprising caspase-3.

21. Kit-of-parts for identifying selective inhibitors of the caspase-3-mediated cleavage of vMLC1 over the caspase-3-mediated cleavage of a peptide containing a functional caspase-3 DEVD cleavage site according to claim 8, comprising the following components:

(i) a first component comprising a peptide containing a functional caspase-3 DEVD cleavage site,

(ii) a second component containing caspase-3, and optionally

(iii) a third component comprising a peptide containing a functional caspase-3 vMLC1 cleavage site.